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Activation of T lymphocytes for the adoptive immunotherapy of cancer.

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BACKGROUND: Adoptive immunotherapy of malignancy involves the passive transfer of antitumor-reactive cells into a host in order to mediate tumor regression. Based on animal models, the transfer of immune lymphoid cells can eradicate widely disseminated tumors and establish long-term systemic immunity. Critical for successful adoptive immunotherapy is the ability to isolate large numbers of immune cells. For clinical therapy, it will require the development on in vitro methods to promote the sensitization and propagation of tumor-reactive cells. However, this is a formidable task since human cancers are postulated to be poorly immunogenic because of their spontaneous origins. RESULTS: Human lymphoid cells for ex vivo activation and subsequent adoptive transfer have been derived from different sources, including peripheral blood, tumor, and lymph nodes. Peripheral blood lymphocytes can be incubated with interleukin 2 to generate lymphokine-activated killer (LAK) cells, which nonspecifically lyse autologous and allogeneic tumor cells in vitro. LAK cell therapy represented the earliest attempt to treat advanced human cancers, with encouraging results documented in patients with renal cell cancer and melanoma. From that experience, the use of more immunologically specific cellular agents with potentially greater therapeutic efficacy has been investigated. One approach uses tumor-infiltrating lymphocytes, which have been characterized experimentally to be more specific in tumor reactivity compared with LAK cells. Other techniques have involved the use of lymphoid cells derived from lymph nodes draining tumors or primed by tumor vaccines. In vitro activation of these cells with tumor antigen or anti-CD3 monoclonal antibody results in the generation of T cells that mediate the rejection of poorly immunogenic tumors in animal studies. These alternate methods are currently being evaluated in clinical studies. CONCLUSIONS: Experimentally, cellular therapy is a potent method to eradicate progressive tumors. Initial clinical studies have demonstrated that this form of therapy is technically feasible and can result in meaningful antitumor responses. Advances in this area will require improved methods to sensitize, isolate, and expand tumor-reactive T cells for adoptive transfer.